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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,708	04/05/1999	GWENYTH JANE FARRAR	MUR-7520	9036

7590 02/27/2003

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EXAMINER
EPPS, JANET L

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/27/2003

33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/155,708	Applicant(s) FARRAR ET AL.9	
	Examin r Janet L Epps-Ford, Ph.D.	Art Unit 1635	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-22,25-27,30-38 and 41-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46-49* is/are allowed.

6)☒ Claim(s) *12-22,25,26,30-38 and 41-45* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *27* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-05-02 has been entered.

Claim Objections

2. Claim 27 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot serve as the basis for another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim 27 was not been further treated on the merits.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 12-14, 18-22, 26, 30, 34-38, 42-43, and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Roth et al. (see entire document)

Claims 12-14, 18-22, 26, 30, 34-38, 42-43, and 45 are drawn to methods for designing a suppression effector and replacement nucleic comprising designing a suppression effector that binds to a portion of a mutant allele, thereby to inhibit the expression of the mutant allele, and

designing a replacement nucleic acid which varies from the mutant allele by having one or more degenerate/wobble sites such that it is not inhibited by the suppression effector, wherein said suppression effector is nucleic acid, ribozyme, or single stranded RNA; and kits comprising these components.

Roth et al. teach a method for treating cancer comprising the use of a pharmaceutical composition comprising an expression construct comprising a first nucleic acid encoding a p53-specific ribozyme, and further comprising a second nucleic acid encoding a functional p53, wherein said second nucleic acid is not cleaved by said ribozyme. According to the disclosure of Roth et al. the term "second nucleic acid transcript" refers to the wt-p53 or functional p53-mRNA that is expressed by the construct and encoded by the second nucleic acid. The second nucleic acid transcript is not cleaved because the ribozyme target site is absent from that transcript (see col. 3, lines 34-43). Additionally, the functional p53 mRNA's of the Roth et al. invention encompass the use of all p53 variants, including wherein, the variations may be purely genetic, i.e., ones that do not result in changes in the protein product. This includes nucleic acids that contain functionally equivalent codons, or codons that encode the same amino acid, such as the six codons for arginine or serine or codons that encode biologically equivalent amino acids (i.e. degenerate codon equivalents, see for example, col. 9, lines 8-45).

The Roth et al. invention also provides a retroviral vector-mediated system that can be used to transduce various hammerhead ribozymes into cancer cells (col. 3, lines 3-6).

Roth et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

5. Claims 12-14, 16-22, 25-26, and 30-38, 42-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Sidransky et al. (see entire document)

The Sidransky et al. invention identifies mutations in a target sequence, such as p53, that are unique to the primary tumor isolated from a subject and metastatic sites derived from the primary tumor. In the tumor cells, the mutated nucleotide sequence is expressed in an altered manner as compared to expression in a normal cell; therefore, it is possible to design appropriate therapeutic or diagnostic techniques directed to this specific sequence. Thus, where a cell-proliferative disorder is associated with the expression of a particular mutated proto-oncogene or tumor suppressor gene nucleic acid sequence, a nucleotide sequence that interferes with the specific expression of the mutated gene at the transcriptional or translational level can be used. The disclosed method utilizes, for example, antisense oligonucleotides and/or ribozymes to block transcription or translation of a specific mutated mRNA, either by masking that mRNA with an antisense nucleic acid or by cleaving it with a ribozyme (col. 12, lines 43-62).

The methods of Sidransky et al. utilizing ribozymes or antisense oligonucleotides specific for the target mutant nucleic acids may also be accompanied by replacement wild type genes (see abstract, col. 13, lines 60-67, and col. 14, lines 63-67). The antisense molecules of Sidransky et al. include those that form duplex structures with the target mRNA, and also those that bind directly to the corresponding target DNA, forming a triplex structure (col. 14, lines 1-20). The ribozymes of Sidransky et al. are single stranded RNA molecules that allow for sequence-specific targeting of mRNA (col. 21-43).

Sidransky et al. also describe various viral vectors that can be used to deliver nucleic acid (i.e. antisense, ribozymes, or replacement genes) to cells for gene therapy purposes (col. 15, lines

18-48). In one particular example Sidransky et al., see Table 2 (col. 20), disclose target regions of mutant p53 that comprise a single nucleotide change in the wobble position of at least one codon that is not found in the wild-type p53 sequence, wherein these target regions are used to design allele specific nucleic acid.

Sidransky et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 12, 15, 21-22, 25-26, 28, 31, 37-38, and 41-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a suppression effector, wherein the suppression effector suppresses the expression of a mutant allele and does not inhibit the replacement nucleic acid that differs from the mutant allele by having one or more degenerate/wobble sites. To the extent that the "suppression effector" encompasses a peptide or antibody, the specification as filed fails to disclose at least one embodiment wherein the suppression effector is either a peptide or antibody and wherein the peptide or antibody functions to inhibit the expression of a mutant allele and does not inhibit a replacement nucleic acid (as defined above).

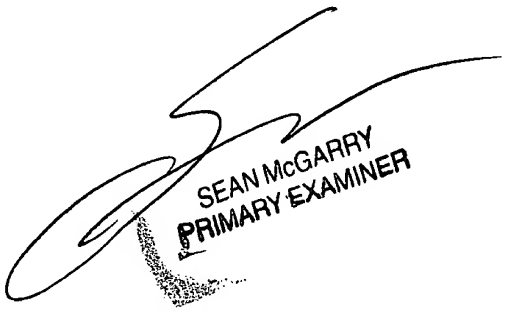
The specification as filed teaches that the suppression effectors of the present invention are directed to sequences in a gene, in transcripts or in protein. The instant claims do not encompass wherein the suppression effectors are targeted to mutant proteins as would be the case for peptides or antibodies, the instant claims requires that the peptide or antibody suppression effector specifically inhibit the expression of a mutant allele while not affecting a replacement nucleic acid. If applicants intended the claims to encompass wherein the suppression effector functions to inhibit the protein product of a mutant allele and not the wild-type protein product, the antibody would not be able to distinguish the two protein products since the amino acid sequences would be the same since they only differ in wobble/degenerate nucleotide sites.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention."

Due to the lack of description in the specification as filed, it is unclear how one of skill in the art would be able to predict the structures of peptides or antibodies which possesses the required functionality as set forth in the instant claims. One of skill in the art would have to resort to trial and error experimentation in order to identify the full scope of compounds encompassed by the claimed invention. In light of the fact that further experimentation is required to identify the full scope of compounds that are useful in the claimed methods and kits, it is apparent that full scope of the claimed invention was not reduced to practice at the time of filing of the claimed invention. Therefore, the full scope of the claimed invention was not "ready for patenting" at the time of filing of the present invention.

Allowable Subject Matter

8. Claims 46-49 are free of the prior art searched.



9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 9:00AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
February 21, 2003

SEAN McGARRY
PRIMARY EXAMINER